AD-A038 957 WISCONSIN UNIV MADISON MATHEMATICS RESEARCH CENTER F/G 6/4
ON MODELLING PATTERN FORMATION BY ACTIVATOR-INHIBITOR SYSTEMS. (U)
FEB 77 P C FIFE DAAG29-75-C-0024
UNCLASSIFIED MRC-TSR-1724 NL

1 OF 1
AD
A038957

END
DATE
FILMED
5-77

ADA038957

MRC Technical Summary Report # 1724

# ON MODELLING PATTERN FORMATION BY ACTIVATOR-INHIBITOR SYSTEMS

Paul C. Fife

12

**Mathematics Research Center**
**University of Wisconsin—Madison**
**610 Walnut Street**
**Madison, Wisconsin 53706**

February 1977

Received December 13, 1976

See Form 1473

DDC
MAY 3 1977
RECEIVED
C

**Approved for public release**
**Distribution unlimited**

DDC FILE COPY

Sponsored by

U. S. Army Research Office
P.O. Box 12211
Research Triangle Park
North Carolina 27709

and

National Science Foundation
Washington, D. C. 20550

UNIVERSITY OF WISCONSIN - MADISON
MATHEMATICS RESEARCH CENTER

# ON MODELLING PATTERN FORMATION BY ACTIVATOR-INHIBITOR SYSTEMS

Paul C. Fife

Technical Summary Report #1724
February 1977

## ABSTRACT

The formation of spatially patterned structures in biological organisms has been modelled in recent years by various mechanisms, including pairs of reaction-diffusion equations

$$u_t = D_1 \nabla^2 u + f(u,v) ,$$
$$v_t = D_2 \nabla^2 v + g(u,v).$$

Their analysis has been by computer simulation. In some cases, $u$ can be interpreted as an activator and $v$ an inhibitor. The following problem is treated: given a "pattern" $u = \varphi(x)$ $v = \psi(x)$, find a system which has it as a stable stationary solution (stability is used in various senses in the paper). This inverse problem is shown to have solutions for reasonable $\varphi$ and $\psi$. The solutions constructed are of activator-inhibitor type with $D_2 > D_1$.

AMS(MOS) Subject Classification: 35K55, 35B35, 92A05

Key Words: Pattern formation, reaction-diffusion equations, parabolic systems, stability of parabolic systems.

Work Unit No: 1 (Applied Analysis)

ACCESSION for
NTIS White Section
DDC Buff Section
UNANNOUNCED
JUSTIFICATION
BY
DISTRIBUTION/AVAILABILITY CODES
Dist. AVAIL. and/or SPECIAL
A

Sponsored in part by the United States Army under Contract No. DAAG29-75-C-0024 and in part by the National Science Foundation under Grant No. MPS-74-06835-A01.

# ON MODELLING PATTERN FORMATION
# BY ACTIVATOR-INHIBITOR SYSTEMS

Paul C. Fife

## 1. Introduction.

The formation of spatially patterned structures in biological organisms has been modelled by various mechanisms in recent years, (see, for example, the survey by Cooke [2] for a description of recent work in the area). Among these modelling attempts have been those using only the processes of chemical reaction and the diffusion of the reacting species. The most common approach to this problem has been that of small-amplitude (linear or nonlinear) analysis of the onset of symmetry-breaking instabilities. I shall not attempt to survey results using this approach, except to say that they were begun by the well-known work of Turing, and include, among others, the work of Gmitro, Othmer, and Scriven, Prigogine, Lefever, and Nicolis, and Segal, Jackson, and Levin. We are concerned here with models yielding large-amplitude patterns. Notable in this regard is the work of Gierer and Meinhardt [6,7,9,10] in Tübingen, and Babloyantz, Hiernaux, Herschkowitz-Kaufman, Nicolis, Prigogine, and others in Brussels [1,8]. See also [4] for models of sharply differentiated structures. These models are generally of the form

(1a) $$u_t = D_1 \nabla^2 u + f(u,v) ,$$

(1b) $$v_t = D_2 \nabla^2 v + g(u,v),$$

Sponsored in part by the United States Army under Contract No. DAAG29-75-C-0024 and in part by the National Science Foundation under Grant MPS-74-06835-A01.

where $u$ and $v$ are the concentrations of two hypothetical reacting substances, and the source terms $f$ and $g$ are derived from assumed reaction schemes. The analysis of these equations has been by computer simulation (except in [4]). The results have indeed indicated the appearance of spatial patterns of various sorts.

The important problem here is, given a stationary spatial pattern of some general description, to find a system of reaction-diffusion equations which will yield that pattern as a stable solution. In addition, one wants to be able to interpret the reaction terms on the basis of some reasonable reaction kinetics. It is this first inverse problem (given a solution, find the equations) that we are concerned about in the present paper. We restrict attention to two-component systems of the form (1) with one space variable $x$ (see §4 for extensions to higher dimensions), and show that for any reasonable given time-independent function $u = \varphi(x)$, there are systems of this type which have a stable stationary solution with $u = \varphi$. Within certain limitations, the function $v = \psi(x)$ can also be prescribed. Systems having the given functions as solution are easy to construct, but stability is an elusive property, and the difficult part is finding systems for which the given solution is stable. For example, the corresponding inverse problem for a scalar equation, $u_t = u_{xx} + f(u)$, the pattern being defined for all $x$, does not have a solution unless the required pattern is monotone; and even then it is structurally unstable, as small changes in $f$ will destroy the pattern [5].

We leave aside the second important task mentioned above, namely the interpretation of $f$ and $g$ on the basis of some reasonable reaction kinetics. The systems we construct have no obvious interpretation in those terms, and for this reason are not likely to be of practical importance as models. At the same time, in constructing model reaction-diffusion systems with only two components, one should not attach overriding importance to having them mirror specific reaction networks involving the two species alone. In fact, the actual mechanism modelled will involve a large number of reacting species (and other entirely different processes as well). One usually justifies the reduction to two species on the basis that various pseudo-steady-state, slow reaction, or other approximations can often be made to effect such a reduction. But when these approximations are introduced, the connection between the source terms $f$ and $g$ and the actual kinetics is necessarily obscured; in particular, $f$ and $g$ do not conform to mass-action kinetics between the two hypothetical species.

The only thing we require of $f$ and $g$ is that they be of activator-inhibitor type, which we define as follows:

<u>Definition:</u> $u$ is an <u>activator</u> for (1) if $f_u > 0$, $g_u > 0$.

$v$ is an <u>inhibitor</u> for (1) if $f_v < 0$, $g_v < 0$.

Thus increasing the amount of $u$ present enhances the production of $u$ and $v$, whereas increasing $v$ has the opposite effect. This requirement was occasioned by the fact that Gierer and Meinhardt's models are of activator-inhibitor type, with the inhibitor diffusing more rapidly than the activator. This latter fact is also true in our scheme, and is necessary to produce stability of the pattern. In fact, one major point of the present paper is an elucidation of how activator-inhibitor mechanisms with different diffusivities may enhance stability.

Up to this point, we have not spoken of boundary conditions which one must impose if (1) is to be solved in a bounded domain in space. They are of little importance in our argument, which is valid for any reasonable boundary conditions, and even for problems on the whole line with no boundary.

The concept of stability we use for most of the results is linearized stability, wherein one examines the spectrum of the operator $S$ obtained by linearizing the right hand side of (1) about the stationary solution $(\varphi,\psi)$. If the spectrum $\Sigma(S)$ has points $\lambda$ with $\mathrm{Re}\,\lambda > 0$, then $(\varphi,\psi)$ is unstable, whereas if all points have $\mathrm{Re}\,\lambda < 0$, it is stable. Marginal stability is when $\Sigma(S)$ has a point with $\mathrm{Re}\,\lambda = 0$, but none with $\mathrm{Re}\,\lambda > 0$. From linear stability, one can often deduce stability in a stricter (such as $C^0$) sense; in particular, that can be done with our examples of patterns on a finite interval, and for our "single-peak" pattern on the whole real line. For any pattern on the whole line, $0$ is always in $\Sigma(S)$, so the most we can hope for in the general case is marginal stability, which is what we in fact obtain. In the case of "single peak" distributions on the whole line, however, for which $\varphi$ is even and monotone for $x > 0$, it turns out that 0 will be an isolated point of $\Sigma(S)$, and we apply a theorem of Sattinger [11] to obtain the result that the stationary solution is stable in the $C^0$ sense. I believe that our results are among the first in which stability is proved for solutions of systems with two or more components, on the entire real line, or of large amplitude patterns on a finite interval.

Some of the results in this paper were announced in [5].

## 2. The inverse problem on a finite interval.

We consider systems of the form

(2a) $$u_t = u_{xx} + f(u,v),$$

(2b) $$v_t = k\, v_{xx} + g(u,v)$$

for functions $u, v$ defined for $x \in [a,b]$, $t \geq 0$. We also prescribe boundary conditions at the endpoints $a$ and $b$, and for definiteness take them to be of no-flux type:

(3) $$u_x(a,t) = u_x(b,t) = v_x(a,t) = v_x(b,t) = 0\ .$$

For a given stationary solution $u = \varphi(x)$, $v = \psi(x)$ of (2), (3), we denote by $S$ the operator obtained by linearizing the right side of (2) about $(\varphi, \psi)$.

$$S\begin{pmatrix}\bar{u}\\ \bar{v}\end{pmatrix} = \begin{pmatrix} \bar{u}_{xx} + f_u(\varphi,\psi)\bar{u} + f_v(\varphi,\psi)\bar{v} \\ \\ k\bar{v}_{xx} + g_u(\varphi,\psi)\bar{u} + g_v(\varphi,\psi)\bar{v} \end{pmatrix} .$$

The operator $S$ is to be considered as acting on $(C^0)^2 \equiv C^0[a,b] \times C^0[a,b]$, with domain the $C^2$ functions satisfying (3). We denote its spectrum by $\Sigma(S)$.

The patterns $\varphi(s)$ which we consider will be in $C^2[a,b]$, and will have the property that $\varphi''$ is a function only of $\varphi$. This latter means that $\varphi$ is even with respect to any local maximum or minimum, so that its graph (see Figure 1) is symmetric with respect to vertical lines through such maxima and minima. To be more precise, the statement is that $\varphi$ can be extended to be defined for all $x$, and the extended graph has those symmetry properties.

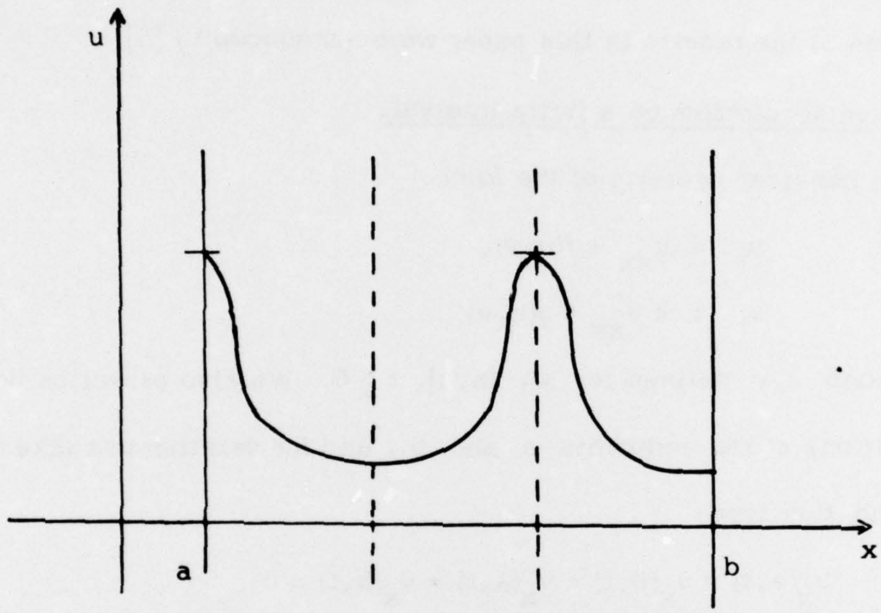


Figure 1. Example of a pattern $\varphi(x)$ with two vertical axes of symmetry (dotted lines).

<u>Theorem 1:</u> Let $\varphi$ be a function in $C^2[a,b]$, satisfying $\varphi'(a) = \varphi'(b) = 0$, and $\varphi''(x) = F(\varphi(x))$ for some $C^2$ function $F$. Let $\psi$ satisfy

(4) $$\varphi = c_1\psi + c_2, \qquad c_1 > 0.$$

Let $k > 1$.

Then there exist functions $f(u,v)$, $g(u,v)$, satisfying $f_u > 0$, $g_u > 0$, $f_v < 0$, $g_v < 0$, such that $(\varphi,\psi)$ is a stable or marginally stable stationary solution of (2), (3). Furthermore $\Sigma(S)$ is discrete and is located entirely in the half-plane $\{\operatorname{Re}\lambda < 0\}$ except possibly for a simple eigenvalue at the origin.

Proof: First consider the case $\varphi \equiv \psi$, so $c_1 = 1$, $c_2 = 0$. For some constant $\sigma$ to be determined later, let

(5a) $$f(u,v) = -F(u) + \sigma(u-v)$$

(5b) $$g(u,v) = -k\, F(v) + k\sigma(u-v).$$

If $\sigma$ is chosen large enough, these will be the required functions. First of all, it is clear that $(u,v) = (\varphi,\varphi)$ satisfies (2), (3). We must show it is a stable or marginally stable solution. Let $L \equiv \frac{d^2}{dx^2} - F'(\varphi(x))$, an operator on $C^0[a,b]$ with domain $\mathcal{D}(L)$ consisting of $C^2$ functions satisfying (3). Then

$$S\begin{pmatrix}\bar{u}\\ \bar{v}\end{pmatrix} = \begin{pmatrix} L\bar{u} + \sigma(\bar{u}-\bar{v}) \\ kL\bar{v} + k\sigma(\bar{u}-\bar{v}) \end{pmatrix}.$$

Let $\varepsilon = 1/k$, and let $P(\lambda,\mu)$ be the polynomial

$$P(\lambda,\mu) \equiv \varepsilon\lambda^2 + \lambda[(1-\varepsilon)\sigma - (1+\varepsilon)\mu] + \mu^2.$$

Then $P(\lambda,L)$ is a fourth order operator with domain functions $h \in \mathcal{D}(L)$ such that $Lh \in \mathcal{D}(L)$; furthermore $\Sigma(P(\lambda,L)) = P(\lambda,\Sigma(L))$ [3, p. 604]. Let

$$\Lambda \equiv \{\lambda : \Sigma(P(\lambda,L)) \ni 0\} = \{\lambda : P(\lambda,\mu) = 0 \text{ for some } \mu \in \Sigma(L)\}.$$

Proposition 1: $\Sigma(S) \subset \Lambda$.

Proof: Let $\lambda \notin \Lambda$. Then 0 is in the resolvent set of $P(\lambda,L)$, and $P(\lambda,L)^{-1}$ is a bounded operator on $C^0[a,b]$. Consider the problem

(6) $$(S - \lambda I)\begin{bmatrix}\bar{u}\\ \bar{v}\end{bmatrix} = \begin{bmatrix}p\\ q\end{bmatrix},$$

with $p,q \in C^0[a,b]$. It can be solved explicitly by the formula

(7a) $$\bar{u} = (L - \sigma - \varepsilon\lambda)P(\lambda,L)^{-1}p + \varepsilon\sigma P(\lambda,L)^{-1}q,$$

(7b) $$\bar{v} = -\sigma P(\lambda,L)^{-1}p + \varepsilon(L + \sigma - \lambda)P(\lambda,L)^{-1}q.$$

It is verified directly, using the fact that $P(\lambda, L)^{-1}$ commutes with $L$ on $\mathcal{D}(L)$, that this formula defines a two-sided bounded inverse $(S-\lambda)^{-1}$. Therefore $\lambda$ is in the resolvent set of $S$. This establishes the proposition.

Proposition 2: $\Lambda$ is a discrete set in the half-plane $\{\mathrm{Re}\lambda \leq 0\}$. Furthermore $\Lambda \subset \{\mathrm{Re}\lambda < 0\}$ unless $0 \in \Sigma(L)$, in which case $\Lambda = \{0\} \cup T$, with $T \subset \{\mathrm{Re}\lambda < 0\}$.

Proof: The discreteness follows from the discreteness of $\Sigma(L)$. We know that $\Sigma(L)$ is real and bounded from above. Let $\sigma$ be so large that $(1-\varepsilon)\sigma - (1+\varepsilon)\Sigma(L) > 0$. Then if $\mu \in \Sigma(L)$ and $\mu \neq 0$, the coefficient of $\lambda$ in the polynomial $P(\lambda, \mu)$ will be positive, so that the sum of the two roots $\lambda_1, \lambda_2$ of $P(\lambda, \mu) = 0$ will be negative. If they are complex conjugates, their common real part must be negative. If they are real, then $\lambda_1\lambda_2 = \mu^2 > 0$, so that they must both be negative. In any case, $\mathrm{Re}\,\lambda < 0$ for any root of $P$.

On the other hand if $\mu = 0 \in \Sigma(L)$, then $P(\lambda, 0)$ has one negative and one $0$ root. This proves the proposition.

We now observe that $f_u > 0$, etc., for large enough $\sigma$. To complete the proof of Theorem 1, we need only show that when $0$ is an eigenvalue of $S$, it is simple. From Proposition 2, we know this happens only when $0$ is an eigenvalue of $L$. Under boundary conditions (3), $L$ has only algebraically simple eigenvalues so there is a unique (up to a scalar factor) nullvector $\theta$. Let $(\chi_1, \chi_2)$ be any nullvector of $S$, so that

$$L\chi_1 + \sigma(\chi_1 - \chi_2) = 0,$$

$$L\chi_2 + \sigma(\chi_1 - \chi_2) = 0.$$

Subtracting, we see that $L(\chi_1 - \chi_2) = 0$, which implies that $\chi_1 - \chi_2 = a\theta$ for some scalar a. Hence $L\chi_1 + \sigma a\theta = 0$. But since 0 is an algebraically simple eigenvalue of $L$, this implies $a = 0$ and $\chi_1 = b\theta$. Hence $(\chi_1, \chi_2) = b(\theta, \theta)$, and S has only one nullvector. A similar argument shows that its algebraic multiplicity is also 1. This completes the proof of the theorem in the case $\varphi = \psi$.

Now if $\varphi \neq \psi$, but is given by (4), we first write the system (2) with f and g given by (5), and the symbol v replaced by w. Then we effect a change of variable $w = c_1 v + c_2$ to obtain the desired system in u and v. This completes the proof.

<u>Remarks:</u> 1. If, instead of (4), $\varphi$ and $\psi$ are related nonlinearly by

$$\varphi = h(\psi)$$

with $h'(\psi) > 0$, then we still obtain a type of nonlinear diffusion system for u and v. The difference is that now (2b) is replaced by

$$v_t = k \frac{(h'(v)v_x)_x}{h'(v)} + g(u,v) .$$

This is obtained by the procedure discussed in the preceding paragraph, except that the change of variable is now $w = h(v)$.

2. The specific form of the boundary conditions (3) was not used; only the fact that $\Sigma(L)$ is bounded from above, discrete, and contains 0, if at all, only as a simple eigenvalue. If this last condition is not fulfilled, then all assertions of the theorem remain true except the final one regarding the simplicity of the eigenvalue at the origin. We may therefore replace (3) by any other boundary conditions for which the above requirements are met.

In particular, periodic boundary conditions could be used. In this case, 0 is always an eigenvalue of $L$, because $L\varphi' = 0$. If $L$ has constant coefficients, it would of course be double, because $L\varphi'' = 0$ as well. But in general, one expects it to be simple.

3. The solution of the inverse problem is certainly not unique; for example, $\sigma$ can be any large enough positive constant. More generally, in place of (5), we may use functions

$$f(u,v) = -F(u) + \sigma(u-v) + (u-v)^2 \tilde{f}(u,v) \tag{8a}$$

$$g(u,v) = -kF(v) + k\tau(u-v) + (u-v)^2 \tilde{g}(u,v), \tag{8b}$$

where $\tilde{f}$ and $\tilde{g}$ are arbitrary, $\sigma$ and $\tau$ are such that there are no points of $\Sigma(L)$ in $[\tau-\sigma,0)$(if $\sigma > \tau$) or in $(0,\tau-\sigma]$ (if $\sigma < t$), and $\tau > \varepsilon\,\sigma + (1+\varepsilon)M$, where $M = \mathrm{Max}(\Sigma(L))$. With such a pair $f,g$, the proof of Theorem 1 goes through with only obvious modifications.

## 3. Patterns on the entire line.

The restriction to a finite interval in the previous section is unnecessary. Let $\varphi$ be a bounded nonconstant function, defined for all $x$, such that $\varphi'' = F(\varphi)$ for some $C^2$ function $F$. Then $\varphi$ will be periodic, peaked or monotone. Here "peaked" means that it has a single maximum or minimum, and approaches a limit as $|x| \to \infty$.

**Theorem 2.** Let $\varphi$ be as described, and let $\psi$ satisfy

$$\varphi = c_1\psi + c_2, \quad c_1 > 0 .$$

Let $k > 1$. Then the conclusions of Theorem 1 hold, except that $\Sigma(S)$ is no longer discrete, and in the periodic case, the eigenvalue at the origin is not necessarily simple. In all cases, $0 \in \Sigma(S)$. In the peaked case, let $\varphi_0 = \lim_{|x|\to\infty} \varphi(x)$. If $F'(\varphi_0) > 0$, then 0 is an isolated point of $\Sigma(S)$ and $(\varphi, \psi)$ is stable in the uniform norm. In the monotone case, let $\varphi_0 = \lim_{x\to -\infty} \varphi(x)$ and $\varphi_1 = \lim_{x\to\infty} \varphi(x)$. If $F'(\varphi_i) > 0$, $i = 0,1$, then $(\varphi,\psi)$ is again stable in the uniform norm.

Proof: The proof of Theorem 1 holds without change, with the same functions (5), except that $\Lambda$ will no longer be discrete, because $\Sigma(L)$ is no longer discrete. In the peaked case with $F'(\varphi_0) > 0$, we know that the points of $\Sigma(L)$ greater than $-F'(\varphi_0)$ are isolated. This follows from [3, p. 1448] and the easily proved fact that any bounded solution of $(L-\lambda)u = 0$ for $\lambda > -F'(\varphi_0)$ must decay exponentially, so is in $\mathcal{L}_2(\underset{\sim}{R})$; hence discrete points of L in this range are eigenvalues of L as an operator in $\mathcal{L}_2(\underset{\sim}{R})$. See also [12]. On the other hand, 0 is always an eigenvalue of L, since $L\varphi' = 0$, and it is simple and has a finite number of nodes. So although $\Lambda$ is no longer discrete, it still lies in the left half-plane except for an isolated point at the origin. The same is therefore true of $\Sigma(S)$. The proof that 0 is a simple eigenvalue of $\Sigma(S)$ proceeds as before.

To prove that $(\varphi,\psi)$ is stable in the $C^0$ sense, we shall use Sattinger's stability theorem [11]. To verify that theorem's hypotheses, it suffices to show that $\Sigma(S)$ lies on the negative real axis, and that the resolvent $(S-\lambda)^{-1}$ satisfies the following estimates for $|\arg \lambda| \leq \pi - \delta < \pi$ and $|\lambda|$ large enough. (In the following, the symbol K will denote several different constants.)

$$\text{(9a)} \qquad \|(S-\lambda)^{-1}h\|_{(C^0)^2} \le \frac{K}{|\lambda|}\|h\|_{(C^0)^2} ,$$

$$\text{(9b)} \qquad \|(S-\lambda)^{-1}h\|_{(C^1)^2} \le \frac{K}{\sqrt{|\lambda|}}\|h\|_{(C^0)^2} .$$

It may be verified directly from the definition of $\Lambda$, and the fact that $\Sigma(L)$ is real, that $\Lambda$, hence $\Sigma(S)$, is real for $\sigma(1-\varepsilon)$ large enough. Therefore $\Sigma(S)$ certainly lies in the required sector.

We now turn to the verification of (9). First, we note that estimates of that form were obtained in [12] for the operator $L$ instead of $S$, provided $F'(\varphi(x))$ approaches its limit exponentially fast as $|x| \to \infty$. But $F(\varphi_0) = 0$, $F'(\varphi_0) > 0$, and $\varphi$ satisfies $\varphi'' - F(\varphi) = 0$, so $\varphi(x) \to \varphi_0$ exponentially as $|x| \to \infty$. Therefore $F'(\varphi(x)) \to F'(\varphi_0)$ exponentially as well.

We may factor $P(\lambda, L)$ as follows:

$$P(\lambda, L) = (L-\mu_1)(L-\mu_2), \quad \mu_i = \tfrac{1}{2}[\lambda(1+\varepsilon) \pm [\lambda^2(1-\varepsilon)^2 - 4\sigma(1-\varepsilon)\lambda]^{\frac{1}{2}}].$$

It is seen that for large $|\lambda|$, $|\mu_i|$ are also large and for some $K$,

$$\text{(10)} \qquad K^{-1}|\lambda| \le |\mu_i| \le K|\lambda| .$$

By (9) and the above mentioned estimate for $(L-\lambda)^{-1}$, we have the following, for large enough $|\lambda|$ in the sector $|\arg\lambda| \le \pi - \delta$:

$$\text{(11)} \qquad \|(L-\mu_i)^{-1}h\|_{C^0(\underset{\sim}{R})} \le \frac{K}{|\lambda|}\|h\|_{C^0(\underset{\sim}{R})} .$$

If $(L-\mu_i)w = h$, we have $w'' = h - \mu_i w + F'(\varphi(x))w$, so from (11),

$$\|(L-\mu_i)^{-1}\|_{C^2(\underset{\sim}{R})} \le K\|h\|_{C^0(\underset{\sim}{R})} .$$

Now

$$\|P(\lambda,L)^{-1}h\|_{C^2} = \|(L-\mu_1)^{-1}(L-\mu_2)^{-1}h\|_{C^2} \leq$$

$$\leq K\|(L-\mu_2)^{-1}h\|_{C^0} \leq \frac{K}{|\lambda|}\|h\|_{C^0},$$

and so

$$\|LP(\lambda,L)^{-1}h\|_{C^0} \leq K\|P(\lambda,L)^{-1}h\|_{C^2} \leq \frac{K}{|\lambda|}\|h\|_{C^0}.$$

These estimates, applied to the explicit representation (7) of $(S-\lambda)^{-1}$, yield

(12) $$\|(S-\lambda)^{-1}\binom{p}{q}\|_{(C^0)^2} \leq \frac{K}{|\lambda|}\|\binom{p}{q}\|_{(C^0)^2}.$$

If $(S-\lambda)\binom{\bar{u}}{\bar{v}} = \binom{p}{q}$, we may again represent $\bar{u}''$ and $\bar{v}''$ in terms of $\bar{u}$, $\bar{v}$, $p$, and $q$, and so obtain

$$\|(S-\lambda)^{-1}\binom{p}{q}\|_{(C^2)^2} \leq K\|\binom{p}{q}\|_{(C^0)^2}.$$

Interpolating between this estimate and (12), we finally obtain

$$\|(S-\lambda)^{-1}\binom{p}{q}\|_{(C^1)^2} \leq \frac{K}{\sqrt{|\lambda|}}\|\binom{p}{q}\|_{(C^0)^2}.$$

This establishes the $C^0$-stability of peaked distributions.

For monotone distributions, $\Sigma(L)$ is discrete above $\mathrm{Max}[-F'(\varphi_0), -F'(\varphi_1)] < 0$. The rest of the argument is the same. This completes the proof of Theorem 2.

<u>Example:</u> Possibly the simplest illustration of single-peak modelling would be for the pattern

$$\varphi(x) = \frac{6e^{x/d}}{(1+e^{x/d})^2} = \psi(x)$$

which represents a peak with maximum of $3/2$ at $x = 0$, $\varphi(\infty) = 0$, and an approximate width $d$, which is arbitrary. Since $\varphi'' + d^{-2}(\varphi^2 - \varphi) = 0$, the model reaction-diffusion equations can be taken to be

$$u_t = u_{xx} + d^{-2}u^2 + (\sigma - d^{-2})u - \sigma v ,$$

$$v_t = kv_{xx} + kd^{-2}v^2 - (\sigma + kd^{-2})v + \sigma u .$$

<u>Remark:</u> In the peaked case, there is another stationary solution of (2) with (5) besides $u \equiv v \equiv \varphi(x)$, namely the constant solution $u \equiv v \equiv \varphi_0$. It is also stable, as the above analysis, together with the fact that $F'(\varphi_0) > 0$, shows. This suggests there may be a third stationary solution which is unstable. In fact, the function $F(\varphi)$ must take on positive and negative values for $\varphi \neq \varphi_0$, so there must be another zero of $F\cdot$, say $\varphi_1$, for which $F'(\varphi_1) < 0$. Then $u \equiv v \equiv \varphi$ is a solution. If $S$ is the linearization about this solution, the above analysis shows its spectrum to be continuous and to extend up to the origin. Very possibly this third solution, though marginally stable in the linearized sense, will turn out to be unstable in the $C^0$ sense.

4. <u>Discussion</u>:

1. Many of the results extend to analogous problems in more than one dimension. For this extension, one replaces $u_{xx}$ and $v_{xx}$ in (2) by $\nabla^2 u$ and $\nabla^2 v$ respectively, and considers patterns $\varphi$ for which $\nabla^2\varphi = F(\varphi)$. Single radially symmetric peaks, for example, have this property, and it is likely that lattices of peaks can also be constructed with it. Then $\Sigma(S)$ again lies on the negative real axis. However, the eigenvalue 0 is no longer necessarily simple.

2. It is clear that the stability proofs given in the preceding two sections depend on

(i) large enough activation by $u$ and inhibition by $v$, and

(ii) the diffusivity $(k)$ of $v$ being larger than that $(1)$ of $u$.

At the same time, it is clear from Remark 3 at the end of §2 that the parameters $\sigma$ and $\tau$ cannot be completely independent for the stability proof to go through. We interpret this by saying that the $u$-activation and the $v$-activation cannot be completely independent.

In our constructed models, there is also a relation between the magnitudes of the activation and the inhibition, and this relation depends on the relative amplitudes of the required distributions $\varphi$ and $\psi$. For simplicity, let us take $c_2 = 0$ in (4); then this relative amplitude will be $c_1$. For $c_1$ not necessarily $1$, the equations corresponding to (8) will be

$$f(u,v) = -F(u) + \sigma(u-c_1 v) + (u-c_1 v)^2 \tilde{f}$$

$$g(u,v) = -\frac{k}{c_1} F(c_1 v) + \frac{k\tau}{c_1}(u-c_1 v) + (u-c_1 v)^2 \tilde{g} .$$

It may be instructive to express all the relations mentioned above directly in terms of some reasonable activation and inhibition parameters. Accordingly, we define the

$u$-activation $\equiv A_u \equiv$ average value of $f_u(\varphi,\psi) \sim \sigma$ (for $\sigma$ large),

$v$-activation $\equiv A_v \equiv$ average value of $g_u(\varphi,\psi) \sim \frac{k\tau}{c_1}$ (for $\tau$ large),

$u$-inhibition $\equiv I_u \sim c_1\sigma$

$v$-inhibition $\equiv I_v \sim k\tau$ .

For our models, then, the following relations exist between the parameters $A_u$, $A_v$, $I_u$, $I_v$, $c_1$, and $k$ :

$$A_u, A_v, I_u, I_v >> 1 ,$$

$$k > 1,$$

(13) $$I_u \sim c_1 A_u ,$$

$$I_v \sim c_1 A_v$$

$$A_v \sim \frac{k}{c_1} A_u .$$

All of these are clear from the preceding except possibly the last. It follows from the fact that although $\sigma$ and $\tau$ were required to be large, their difference had to be small enough. So we can write $\sigma \sim \tau$ .

This is no demonstration that the relations (13) are always necessary to produce stable patterns; nevertheless it seems reasonable to use them as one possible guide in constructing other models, not of the form given in the present paper.

## References


1. A. Babloyantz and J. Hiernaux, Models for cell differentiation and generation of polarity in diffusion-governed morphogenetic fields, Bull. Math. Biol. (to appear).

2. J. Cooke, The emergence and regulation of spatial organization in early animal development, Ann. Rev. Biophysics and Bioengineering 4 (1975), 185-217.

3. N. Dunford and J. T. Schwartz, Linear Operators, Parts I and II, Interscience, New York, 1957 and 1963.

4. P. C. Fife, Pattern formation in reacting and diffusing systems, J. Chem. Phys. 64 (1976), 554-564.

5. P. C. Fife, Stationary patterns for reaction-diffusion equations in: Papers on Nonlinear Diffusion, Proceedings of NSF-CBMS Regional Conference on Nonlinear Diffusion, Research Notes in Mathematics, Pitman, London, to appear.

6. A. Gierer and H. Meinhardt, A theory of biological pattern formation, Kybernetik 12 (1972), 30-39.

7. A. Gierer and H. Meinhardt, Biological pattern formation involving lateral inhibition, Lectures on Mathematics in the Life Sciences, Vol. 7, American Math. Soc. (1974), 163-183.

8. M. Herschkowitz-Kaufman and G. Nicolis, Localized spatial structures and nonlinear chemical waves in dissipative systems, J. Chem. Phys. 56 (1972), 1890-1895.

9. H. Meinhardt, The formation of morphogenetic gradients and fields, Ber. Deutsch. Bot. Ges. 87 (1974), 101-108.

10. H. Meinhardt and A. Gierer, Applications of a theory of biological pattern formation based on lateral inhibition, J. Cell. Sci. 15 (1974), 321-346.

11. D. H. Sattinger, On the stability of waves of nonlinear parabolic systems, Advances in Math (to appear).

12. D. H. Sattinger, Weighted norms for the stability of travelling waves, preprint.

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

# REPORT DOCUMENTATION PAGE

READ INSTRUCTIONS BEFORE COMPLETING FORM

**1. REPORT NUMBER**
1724 (14) MRC-TSR-1724

**2. GOVT ACCESSION NO.**

**3. RECIPIENT'S CATALOG NUMBER**
(9) Technical

**4. TITLE (and Subtitle)**
(6) ON MODELLING PATTERN FORMATION BY ACTIVATOR-INHIBITOR SYSTEMS

**5. TYPE OF REPORT & PERIOD COVERED**
Summary Report - no specific reporting period

**6. PERFORMING ORG. REPORT NUMBER**

**7. AUTHOR(s)**
(10) Paul C. Fife

**8. CONTRACT OR GRANT NUMBER(s)**
(15) DAAG29-75-C-0024, NSF-MPS-74-06835-A01

**9. PERFORMING ORGANIZATION NAME AND ADDRESS**
Mathematics Research Center, University of Wisconsin
610 Walnut Street
Madison, Wisconsin 53706

**10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS**
#1 - Applied Analysis

**11. CONTROLLING OFFICE NAME AND ADDRESS**
See Item 18 below (12) 21p.

**12. REPORT DATE**
(11) Febr[redacted]77

**13. NUMBER OF PAGES**
17

**14. MONITORING AGENCY NAME & ADDRESS (if different from Controlling Office)**

**15. SECURITY CLASS. (of this report)**
UNCLASSIFIED

**15a. DECLASSIFICATION/DOWNGRADING SCHEDULE**

**16. DISTRIBUTION STATEMENT (of this Report)**

Approved for public release; distribution unlimited.

**17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)**

**18. SUPPLEMENTARY NOTES**

U. S. Army Research Office
P.O. Box 12211
Research Triangle Park,
North Carolina 27709

National Science Foundation
Washington, D. C. 20550

**19. KEY WORDS (Continue on reverse side if necessary and identify by block number)**

Pattern formation, reaction-diffusion equations, parabolic systems, stability of parabolic systems

**20. ABSTRACT (Continue on reverse side if necessary and identify by block number)**


The formation of spatially patterned structures in biological organisms has been modelled in recent years by various mechanisms, including pairs of reaction-diffusion equations

$$u_t = D_1\nabla^2 u + f(u,v)\,,$$

$$v_t = D_2\nabla^2 v + g(u,v).$$

u sub t, v sub t — Laplacian

Their analysis has been by computer simulation. In some cases, $u$ can be interpreted as an activator and $v$ an inhibitor. The following problem is treated: given a "pattern" $u = \varphi(x)$ $v = \psi(x)$, find a system which has it as a stable — next page


DD FORM 1 JAN 73 1473 EDITION OF 1 NOV 65 IS OBSOLETE

UNCLASSIFIED 221 200

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

stationary solution (stability is used in various senses in the paper). phi psi
This inverse problem is shown to have solutions for reasonable $\varphi$ and $\psi$.
The solutions constructed are of activator-inhibitor type with $D_2 > D_1$.